REMARKS

Status of the claims

Claims 1-3, 5-10 and 12-19 are pending. Claims 1-3, 5-10 and 12-19 are rejected. Claims 8, 13-14 and 19 are amended. Claims 4, 11, 16-18, and 20 are/were canceled. No new matter is added.

Claim amendments

Claim 13 is amended to incorporate the limitations of dosage range in claim 16, the limitation of a human in claim 17 and the limitation of multiple sclerosis in claim 18 to overcome rejections under 37 C.F.R. 102(b) & (e), as discussed *infra*. Claims 8, 14 and 19 are amended to correct claim language. Claims 16-18 are canceled. No new matter is added.

Objections to the Drawings

As indicated by the Examiner in Paper No. 5, mailed December 17, 1997, the drawings for the above-referenced application were declared informal when filed. Applicant encloses herewith a set of drawings in compliance with 37 C.F.R. 84 for review by the Draftsman.

Corrected Combined Declaration and Power of Attorney

Applicant submits herewith a Combined Declaration and Power of Attorney in compliance with 37 C.F.R. 1.63 correctly claiming priority under 35 U.S.C. 120 to prior applications 08/408,271 and 08/226,631.

The 35 U.S.C. §102(b) rejection

Claims 13-15 and 17-18 are rejected under 35 U.S.C. §102(b) as being anticipated by **Cummins** (U.S. Patent No. 5,019,382). Applicant respectfully traverses this rejection.

The Examiner maintains that claims 13-15 and 17-18 are anticipated by **Cummins** for the same reasons discussed by the Board of Patent Appeals and Interferences. Applicant submits that **Cummins** suggests contacting the oropharyngeal mucosa with interferon to potentiate disease-corrective immune responses in vertebrates with immuno-resistant disease states characterized by apparent hyper- or hypoactive immune system function, e.g., autoimmune disorders having chronic tissue degenerative inflammation such as multiple sclerosis. A dosage of about 0.1 to about 5 IU/lb is administered in a solution or in a novel solid unitary

dosage form adapted to be dissolved in saliva when placed in the mouth (Abstract).

Applicant has amended claim 13 to incorporate the high dosage ranges of about 50 I.U./kg to about 25,000 I.U./kg recited in dependent claim 16. **Cummins** specifically teaches low dose administration.

Applicant's invention, as recited in amended claim 13, is to a method of reducing inflammation associated with multiple sclerosis in a human by ingesting a type one interferon. **Cummins** merely and only provides what a person having ordinary skill in this art would consider to be superficially anecdotal, non-scientific evidence that interferon treats multiple sclerosis. Without enabling scientific data recognized as such by one of ordinary skill in the art, **Cummins** has not demonstrated possession of the Applicant's invention, for example, a method of reducing inflammation associated with multiple sclerosis.

Cummins administered interferon to a single female subject with multiple sclerosis for 21 days. **Cummins** states that the subject had an extensive neurologic workup elsewhere prior to treatment but does not state what the neurologic workup entailed. The patient was treated by holding a solution of interferon in the

mouth up to about a minute twice daily for 21 days. **Cummins** states that the patient had no recurrence of neurologic symptoms for the nine months (col. 12, ll. 40-45). **Cummins** is silent as to how this was determined, i.e., no indication is given whether this determination was made via another neurologic workup or simply that these symptoms were not evident to the subject.

It is well known that multiple sclerosis is predominantly a relapsing-remitting disease. Although inflammation is one component of multiple sclerosis, plaque development in myelin, i.e., demyelinization, determines what symptoms are presented during an attack. Symptoms of an attack spontaneously decrease and may even disappear after several days to several weeks. New attacks appear unpredictably after periods of recovery lasting months to years. An MRI can indicate the location of plaque formation. Additionally, it is known in the art that natural killer cell activity is deficient in multiple sclerosis and correlates with disease severity and that this activity can be normalized with interferon treatment (pg. 3, ll. 16-18).

Applicant has demonstrated that ingested interferon reduces inflammation in chronic experimental autoimmune encephalomyelitis (EAE), which is a well known model of multiple

sclerosis humans. In experimental autoimmune encephalomyelitis mice given ingested interferon after the initial attack showed significantly less inflammatory foci upon histological examination (pg. 25, ll. 12-17; Fig. 1). Additionally, ingested interferon consistently decreased Con A induced IFN-γ, a mediator of inflammation, in spleen cells, e.g., mock spleen 2,180 ng/ml vs. interferon spleen 1,100 ng/ml and 247 ng/ml vs. 143 ng/ml (pg. 26, ll. 3-7).

In humans serum ICAM-1 and IFN-γ were used as a markers of inflammation. Subjects with early relapsing-remitting multiple sclerosis demonstrated decreased levels of soluble serum ICAM-1 after ingesting different doses of interferon compared to levels prior to ingestion (page 15, ll. 9-12; page 55, ll. 12-20; Figure 14).

Applicant submits that the "clinical trial" conducted in **Cummins** based on only one subject and containing no specific clinical data, either before or after treatment is presented, is statistically insignificant and therefore, medically insignificant. Indeed, the results presented in **Cummins** seem to have been determined by subjective assessment only. Absent scientifically relevant clinical data about abatement of symptoms or even how the

symptoms presented initially and further considering that it is known in the art that (1) demyelinization and inflammation are separate indicators; 2) demyelinization determines what symptoms are present during an attack; and 3) that interferon is known to reduce severity of attacks by normalizing NK cell activity, one of ordinary skill in the art would not find that **Cummins** has enabled a method of reducing inflammation associated with multiple sclerosis by administering interferon to the oropharynx and more particularly by administering interferon via ingestion, as recited in amended claim 13.

Applicants strongly maintain that **Cummins** does not teach ingestion of interferon, as disclosed in the instant specification. At the time of the instant invention, **Cummins** teaches the general knowledge in the art was that interferon, as a protein, would not survive the enzymes in the digestive process (col. 2, ll. 47+) and would not be transported across the gut mucosa (**Lecce** *et al.* J Mol Biotherapy 2:211, pg. 4 of 6 (1990), reference enclosed). Applicant has demonstrated in the instant invention that interferon can induce a response when delivered to the stomach and small intestine and interacts with the gut mucosa, such as in a GALT-mediated response (pg. 64, ll. 18 to pg. 65, ll, 19).

Furthermore, although in its Decision on Appeal for the instant application, the Board of Patent Appeals defined ingest as "to take or absorb (food) into the body" (The American Heritage College Dictionary, Fourth Ed. Houghton Mifflin co. (2002)), Applicants respectfully submit that the Board of Patent Appeals did not consider that this definition encompasses all life forms capable of ingestion. Lower life forms may absorb food into the body, however, higher forms of animal life and humans ingest or take food into the body by swallowing. The electronic World Book Dictionary (World Book, Inc. 2001) better defines ingestion as "to take food or other substance into the body for digestion".

Although oral administration for the purposes of ingestion, as defined in the instant specification, necessarily requires the interferon initially must be delivered through the oropharynx, the interferon does not remain in the oropharynx for sufficient time to contact and interact effectively with the oral mucosa for uptake and delivery to a systemic location, as taught in **Cummins** (col. 4, ll. 13-18 & 37-41). Additionally, **Cummins** demonstrated a therapeutic effect of type I interferon administered to the oropharynx of a patient in **Koech** *et al.* (pg. 2 of 5; reference provided) or to an animal in **Lecce** *et al.* (pg. 2 of 6). In both instances the interferon,

whether in powder or in solution was held in the mouth for a specified period of time.

Cummins teaches that it is critical that the interferon is administered in a dosage form adapted to assure maximum contact with the oropharyngeal mucosa of the human or animal (col. 4, ll. 37-41). As disclosed in the Applicant's specification, the interferon effectively bypasses the oropharynx. Subjects ingested the interferon by taking the drug into the mouth and **immediately swallowing** (Applicants emphasis) with at least 150 mls of water, (pg. 11, ll. 9-10; pg. 14, ll. 6-8). This is not holding the interferon, in any form, in the mouth to contact and absorb into the oral mucosa, swallowing with a quantity of water precludes such contact.

Upon examination of **Cummins** and with the general beliefs and knowledge in the art at that time, one of ordinary skill in the art must conclude that systemic absorption of a substance, such as interferon, through the oral mucosa is not ingestion. **Cummins** specifically states that his discovery is that interferon was taken up by the oral/pharyngeal mucosa and, as such, one of ordinary skill in the art must ensure that the interferon contacts the oral and/or pharyngeal mucosa (col. 4, ll. 13-18 & 37-41). **Cummins** teaches that in clinical trials patients retained the interferon in the mouth

about 15 secs to a minute, depending on the pharmaceutical carrier for the interferon to be absorbed. After sufficient retention in the mouth, the solution was either swallowed or discharged from the patient's mouth (col. 12, ll. 25-29; Claims 1 & 12).

One of ordinary skill in the art may infer that, as the solution may be spit out, no interferon or a negligible amount was remaining and that swallowing is merely an alternative means of eliminating the saliva and/or remaining solution from the mouth with no benefit provided. This inference is supported by the general belief that interferon would not survive the gastrointestinal environment and further by **Cummins** who hypothesizes that the oral cavities of humans and animals contain receptors for interferon which, when bound, are involved in an immunomodulatory process resulting in a generalized elevation of immunocompetence in the host (**Lecce** *et al.* J Mol Biotherapy 2:211, pg. 5 of 6 (1990)).

At a minimum, in view of amending claim 13 to specifically recite the higher dosages recited in claim 16, **Cummins** no longer teaches every element of the instant invention. Claims 14-15, and 17-18 depend from claim 13. Claims 17-18 are incorporated into claim 13 and canceled. Claims 14-15 further limit the invention as recited in amended claim 13 with respect to types of interferon.

Applicant submits that if, as amended, independent claim 13 is not anticipated by **Cummins**, then the incorporation of dependent claims 14-15 therein also are not anticipated by **Cummins**.

For a valid §102 rejection, the prior art references must contain each element of the claimed invention. Absent teachings of the specific dosage range recited herein and in view of Applicant's arguments that **Cummins** does not teach reducing inflammation associated with MS using interferon nor ingestion of interferon, **Cummins** does not teach each element of Applicant's claimed invention. Therefore, as these references are not valid prior art against the instant application under 35 U.S.C. §102 and in view of the preceding amendments and remarks, Applicant respectfully submits that the cited reference does not anticipate claims 13-15 and 17-18 under 35 U.S.C. §102(b). Accordingly, Applicants respectfully request that the rejections of claims 13-15 and 17-18 under 35 U.S.C. §102(b) be withdrawn.

Claims 1-3, 5-10 and 12-19 are rejected under 35 U.S.C. §102(e) as being anticipated by **Sobel** (U.S. 5,780,021). Applicant respectfully traverses this rejection.

The Examiner states that **Sobel** teaches the oral administration (col. 13, ll. 10+) of a type I interferon for autoimmune diseases, including diabetes, in the same doses claimed herein (col. 13, ll. 10+; col. 2, ll. 5-30; col. 4, ll. 10-25). The species to be treated are taught (col. 4; col. 11, ll. 35+). Additionally, the Examiner argues that **Sobel** teaches that the treatment reduces inflammatory response (col. 10) and that it inhibits recurrent diabetes (col. 11, ll. 20).

In U.S. Patent No. 5,780,021 **Sobel** states generally that administering an effective amount of a Type I interferon or a hybrid or analog or mixture thereof to a mammal prevents or treats autoimmune disorders by (Abstract; col. 1, ll. 46-49). **Sobel** teaches that doses may range from 1×10^5 to 75×10^6 units, but may be 1×10^4 units or lower (col. 4, ll. 10-17). **Sobel** makes a general statement that the interferon may be administered orally, intravenously, intramuscularly, intraperitoneally, or subcutaneously (col. 4, ll. 24-28). **Sobel** further generalizes that interferons may inhibit recurrent diabetes in transplanted pancreas or islet cells in a patient having Type I diabetes (col. 11, ll. 20-22).

Sobel specifically teaches that intraperitoneal delivery of 400,000 units of a hybrid interferon lowered the incidence of

diabetes in DP-BB rats as demonstrated by survival curve analysis (col. 9, ll. 59 to col. 2, ll. 42). Rats were given interferon at approximately 40 days of age and diagnosed as diabetic when blood glucose levels exceeded 200 mg % on two consecutive days and were then sacrificed (col. 10, ll. 1-5). In a second experiment, 100,000 units of interferon were administered I.P. at 35-40 days to Group 2 and at 28-30 days to Group 3 with Group 1 as saline control. Group 2 animals were given I.P. interferon for six weeks and sacrificed at the end of the experiment and Group 3 animals received I.P. interferon until sacrifice upon detection of diabetes (col. 10, ll. 16, 27). Incidence of diabetes in Groups 2-3 was lower than control.

Applicant's invention, as recited in claims 1, 8, 13 and 19, are to methods, via ingested interferon, of treating an autoimmune disease, of decreasing the severity or frequency of a relapse of multiple sclerosis in a human, of reducing inflammation associated with multiple sclerosis in a human and of reducing levels of a cytokine in an individual having multiple sclerosis, respectively. Importantly, **Sobel** does not delineate multiple sclerosis as one of the species encompassed by the term "autoimmune disease" (col. 1, ll. 13-23).

Applicant has demonstrated that interferon exhibits a positive effect on established EAE in animals and on multiple sclerosis in humans, as described *supra* in **Cummins**. After an initial attack of EAE, mice fed 100 units interferon underwent a delayed single attack without residual neurological deficit compared to mock fed EAE mice which had two relapses within the same time frame with a resultant neurological deficit. The ingested interferon blunted the severity of the attack and decreased the group clinical score between the initial attack and relapse in treated mice (pg. 24, ll. 8-21). Additionally, the number of parenchymal inflammatory foci in spinal cord tissue was reduced (pg. 25, ll. 13-15). Furthermore, Applicant has demonstrated that ingested interferon decreases levels of cytokines in humans, e.g. IFN-γ and ICAM-1, as discusses *supra* with **Cummins**, and TGF-β, IL-2, IL-10 (pg. 14, ll. 20 to pg. 15, ll. 21; pg. 55, ll. 1-24; Figs. 13-14).

In considering Applicant's claim 1, **Sobel** does not teach treatment of diabetes mellitus or any other inflammatory disease, but rather that the incidence of diabetes is reduced and the onset slightly delayed in DP-BB rats when interferon is administered IP prior to clinical appearance of the disease compared to DP-BB rats administered saline (Figs. 1-2). To treat any disease one of ordinary

skill in the art must deal with the existing disease to relieve it or, optimally, to cure it. **Sobel's** actions were to delay the onset of diabetes mellitus in a smaller incident population via injected interferon.

Sobel has not established that injected interferon treats clinically apparent diabetes. The disease may not have occurred in some animals, but the rest of the population administered interferon did become diabetic albeit at a slower rate than control animals. Even if one could argue that this amount to prevention of diabetes, it certainly is not commensurate with treating diabetes. A showing that, after discontinuing the interferon, no more rats became diabetic over an additional 40 days does not demonstrate treatment of diabetes. **Sobel** does not compare either the blood glucose or degree of mononuclear infiltration of islet cells of these rats at incidence of the disease with that at sacrifice. Nor does **Sobel** compare mononuclear infiltration of rats sacrificed at onset of clinically apparent diabetes with those rats sacrificed more than 40 days after treatment was discontinued. Blood glucose levels were monitored in all rats only until diabetes became apparent upon reaching a 200 mg % blood glucose level.

Again **Sobel** surmises further that interferon can inhibit recurrent diabetes in transplanted pancreas and islet tissue in an individual already diagnosed with diabetes mellitus. **Sobel** bases this on histopathologic examination of the pancreas which showed less mononuclear infiltration within the islet compared to control. Thus, **Sobel** states that interferon appears to reduce the inflammatory response within the islet rather than inhibiting the islet destructive activity of immune cells within the islet. None of these teachings of **Sobel** are applicable to multiple sclerosis.

With regard to Applicant's claim 8, demyelinization in the white matter of the brain and spinal cord determines the frequency and severity of symptoms and relapse in multiple sclerosis. Applicants have demonstrated that ingested interferon reduces the clinical severity of the relapse attack based on observable degrees of hind limb weakness and/or paraplegia and ataxia (pg. 18, ll. 16-22). **Sobel** specifically teaches inhibiting recurrence of diabetes in transplanted tissue in individuals with diabetes.

Applicant's claim 13, as amended, is drawn to reducing multiple sclerosis associated inflammation in a human via ingested interferon. **Sobel** may teach that mononuclear infiltration of pancreatic tissue is less than control at the time of incidence of

diabetes, but **Sobel** does not teach that established mononuclear infiltration of pancreatic tissue is reduced after clinical appearance of the disease within either the injected population or the control population. **Sobel** does not teach multiple sclerosis nor, for that matter, teaches that inflammation is reduced in any other autoimmune disease with an inflammatory response. Diabetes and relapsing-remitting multiple sclerosis are significantly different diseases occurring in very different tissues with completely different biochemical and molecular bases.

Compared with Applicant's claim 19, **Sobel** most assuredly does not teach reducing cytokine levels in an individual having multiple sclerosis via ingested interferon. **Sobel** only examines pancreatic tissue for presence of mononuclear cells as an indication of inflammation. **Sobel** does not teach that levels of cytokines correspond to severity of the disease nor the *in vitro* or *ex vivo* analysis of cytokine secretion in mitogen-activated spleen cells or peripheral mononuclear cells before or after administration of IP interferon to demonstrate such effect, as discussed in the instant application *supra*.

Applicant submits that the examples provided in **Sobel** do not provide an enabling disclosure such that a skilled artisan could

take the teachings in **Sobel** in combination with his own knowledge of the particular art and be in possession of the invention. **Sobel** teaches decreasing the incidence and delaying the onset of diabetes in a subject only. No disclosure is provided for treatment of established disease and certainly no teaching is present for treating multiple sclerosis or reducing any clinical effects associated therewith.

Furthermore, a single statement that the interferons may be administered orally also does not provide an enabling disclosure for oral administration. **Sobel** provides no guidance to one of ordinary skill in the art as to how to orally administer the interferons to the gut for ingestion to circumvent the problem of enzyme degradation of the interferon in the stomach, as was discussed *supra*. Administration via parenteral injection cannot be equated with oral administration for ingestion.

Applicant's specification demonstrates that interferon administered subcutaneously in the animal model of experimental allergic neuritis had no more effect than in untreated animals compared to ingested interferon (pg. 34, ll. 10-24; Fig. 6). Also, in U.S. Patent No. 5,019,382, **Cummins** discloses that interferons have been administered intramuscularly and intradermally, but seldom

intravenously because of substantial adverse effects even from highly purified isolates. Additionally, prior to **Sobel**, **Cummins** taught that parenteral administration of high dose huIFN-alpha caused a flu-like syndrome with significant symptoms in HIV-1 positive patients (**Koech** *et al.* Mol Biother 2:91 (1990); pg. 1 of 5, reference enclosed).

Sobel only has demonstrated to one of ordinary skill in the art that intraperitoneally administered interferons do exhibit a positive effect on reducing the incidence of diabetes. At best, **Sobel** teaches intraperitoneal injection of type I interferon. **Sobel** also may provides guidance to one of ordinary skill in the art for intramuscular injections of type I interferons, but does not provide an enabling disclosure for oral administration for ingestion.

Regardless of the dosage used, **Sobel** simply teaches that interferon may be formulated in any pharmaceutical composition standard in the art such as used for any other orally administered drug and, optionally, may be coated by any standard means to mask taste or to delay availability to gastrointestinal juices (col. 12, ll. 7-15; col. 13, ll. 11-32). Applicant submits that this is not an enabling disclosure, but rather a generic boilerplate review of pharmaceutical compositions for any orally administered drug. Regardless of

formulation, eventually the interferon would be exposed to the gut environment. Applicant strongly reiterates, as stated *supra*, that at the time of filing **Sobel** the knowledge and belief in the art was that interferons would not survive digestive enzymes, as taught *supra* by **Cummins** (col. 2, ll. 47+), nor could be transported across the gut mucosa for systemic delivery (**Lecce** *et al.* J Mol Biotherapy 2:211, pg. 4 of 6 (1990)).

It is not a trivial matter to administer drugs, particularly if it has been demonstrated that specific scientific problems need to be overcome for efficacious delivery depending upon the route of administration and that, based on the knowledge at the time, not all routes of administration may be viable to achieve a therapeutic effect. Additionally, an alternate route of administration may not be able to correct the problems of another route. Thus, given the state of this particular art and what was generally believed about administration of interferon to the gut, one of ordinary skill in the art would not consider a sole statement that interferon may be administered orally as providing sufficient teaching to practice such administration.

Applicant submits that in view of the state of the art at the time of filing the instant application and the lack of any enabling

disclosure for oral administration, i.e., ingestion, of Type I interferon, **Sobel** can not anticipate independent claims 1, 8, 13 and 19. Claims 2-3 and 5-7, 9-12, and 14–15 depend from independent claims 1, 8 and 13, respectively. Claims 16-18 are canceled. These claims further limit the invention as recited in claims 1, 8 and 13 with respect to types of interferon, administration to a human and the types of autoimmune diseases. Applicant submits that if independent claims 1, 8 and 13are not anticipated by **Sobel**, then **Sobel** cannot anticipate claims 2-3 and 5-7, 9-12, and 14–18.

For a valid §102 rejection, the prior art references must contain each element of the claimed invention. In view of Applicant's arguments that **Sobel** does not teach ingestion of interferon to treat autoimmune diseases nor does not teach the delay in or reduction in level of clinically manifested symptoms of multiple sclerosis, **Sobel** does not teach each element of Applicant's claimed invention. Therefore, as these references are not valid prior art against the instant application under 35 U.S.C. §102 and in view of the preceding amendments and remarks, Applicant respectfully submits that the cited reference does not anticipate claims 13-15 and 17-18 under 35 U.S.C. §102(e). Accordingly, Applicants respectfully request that the

rejections of claims 13-15 and 17-18 under 35 U.S.C. §102(e) be withdrawn.

The 35 U.S.C. §103(a) rejection

Claims 1-3, 5-10 and 12-19 are rejected under 35 U.S.C. §103(a) as being obvious over **Sobel** and **Cummins**. Applicant respectfully traverses this rejection.

The Examiner states that **Sobel** teaches all the limitations of the claims listed and discussed *supra*. Furthermore, **Cummins** teaches all the limitations of the claims except the alternate day dosing. The Examiner further states that **Cummins** does teach a single or multiple daily dose regimen and a staggered regimen of 1-3 days per week or month as an alternative to daily dosing (col. 5, ll. 50-55). With such flexibiity as taught by the reference and that it is common in the art to employ such a regimen instead of continuous dosing, it would have been obvious to one of ordinary skill in the art to adopt an alternate day dosing and administer IFN as shown by **Cummins** for MS. The Examiner further points out that even though **Sobel** teaches the same amounts, the reference further states that the precise amount will depend on the judgement of the attending

physician based on considerations of age, weight and condition of the patient.

Applicant's arguments that **Sobel** does not anticipate the instant invention, as recited in claims 1-3, 6-11 and 11-19 are the same. Applicant respectfully points out that alternate day dosing is not a limitation recited in any of claims 13-19 cited in this obviousness rejection. Additionally, as discussed *supra*, **Cummins** does not teach the dosage ranges recited in claims 1, 8, 13, nor 19, as previously or currently amended. Thus, excluding the alternate day dosing, **Cummins** does not teach all of the other limitations of claims 1-3, 6-11 and 13-19.

Applicant maintains that neither **Sobel** nor **Cummins** teaches oral administration for ingestion of Type I interferons. As such, any motivation for one of ordinary skill in the art to combine alternate day dosing, as suggested in **Cummins**, with **Sobel** is moot because, absent teaching ingestion of Type I interferons in both, not all the elements of the instant invention are present in the combination. For the same reasons **Cummins** can not render claims 1-3, 6-11 and 13-19 obvious. Furthermore, the combination of **Sobel** and **Cummins** cannot remedy the deficiencies in either

because **Sobel** and **Cummins** both lack the same element of the invention.

As stated *supra*, claims 2-3 and 5-7, claims 9-10 and 12 and claims 14-15 depend from independent claims 1, 8 and 13, respectfully. Claims 16-18 are canceled. If the combination of **Sobel** and **Cummins** cannot render independent claims 1, 8, 13, and 19 obvious, then neither can the combination render claims 2-3 and 5-7, claims 9-10 and 12 and claims 14-18 obvious.

Obviousness requires a teaching of all the elements by the prior art with a motivation or suggestion to combine the prior art with a reasonable expectation of success. At a minimum, the combination of **Sobel** and **Cummins** lacks teaching oral administration for ingestion of interferon. Thus, in view of the above claim amendments and remarks, the invention as a whole was not obvious to one of ordinary skill in the art at the time the invention was made. Accordingly, Applicants respectfully request that the rejection of claims 1-3, 5-10 and 12-19 under 35 U.S.C. §103(a) be withdrawn.

This is intended to be a complete response to the Office Action mailed July 30, 2003. If any issues remain outstanding, the Examiner is respectfully requested to telephone the undersigned

attorney of record for immediate resolution. Applicant believes no fees are due, however, if this in error, please debit any fees due from Deposit Account No. 07-1185 on which Applicant's counsel is allowed to draw.

Respectfully submitted,

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